

Prevalence of Neutralizing Antibody to Respiratory Syncytial Virus in Sera from Mothers and Newborns Residing in The Gambia and in the United States

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The prevalence of maternal respiratory syncytial virus (RSV)-neutralizing antibodies has been documented in developed countries, but there is little information from developing countries. We assessed the prevalence of RSV-neutralizing antibody in sera from Gambian women and their newborns and compared them with their American counterparts during a similar period. The geometric mean titers of maternal antibodies to RSV subgroup A in the two populations were similar, while titers of antibodies to RSV subgroup B in Gambian mothers were significantly higher (8.7 ± 1.4 versus 7.9 ± 1.3 [mean \pm standard deviation], $P < 0.001$). The titers of neutralizing antibody in newborns in both populations correlated with the neutralizing-antibody titers of their mothers. Thus, the status of neutralizing antibody to both major RSV subgroups was comparable among infants and mothers in a developing country, The Gambia, and those in a developed country, the United States.

Acute respiratory infection is a major cause of childhood morbidity and mortality throughout the world, accounting for about 4 million of the 14 million deaths annually among children under 5 years of age (2, 12). Most of these deaths occurred in developing countries, where respiratory syncytial virus (RSV) usually is reported as the most common viral cause of acute respiratory infection in children (1, 2, 10). The severity of RSV infection is influenced by age, sex, nutritional status, and environmental conditions such as overcrowding and air pollution (2, 4, 6). The preponderance of severe RSV disease in young infants may be due in part to immaturity of the immune system, low levels of maternal antibodies, small airway size, and other factors. Recent observations suggest that neutralizing-antibody levels between 1:300 and 1:400 (8.2 to 8.6 log₂) are protective within the first months of life in term infants (6).

The Gambia is a small West African country with an approximate population of 1 million, located at a latitude 12° north of the equator. The climate consists of a wet season from July to October, a cool season from November to February, and a hot, dry season from March to June. In The Gambia, childhood diseases and mortality show marked seasonality (3). During the past 2 years, a peak of acute respiratory infection in the wet season has been due to RSV (20).

To the best of our knowledge, no study from a developing country has addressed the prevalence of RSV-neutralizing antibodies in sera from women and their newborn infants. In this study, the prevalence of neutralizing antibody to the two major RSV subgroups (RSV/A and RSV/B) for Gambian mothers

and their newborns was determined and compared with that for women and their newborns living in an industrialized setting, Houston, Tex.

The study was approved by the Institutional Review Boards of Baylor College of Medicine and the Medical Research Council Scientific Committee. In The Gambia and Houston, consent was obtained from pregnant mothers attending antenatal clinics or at parturition. The period of the study in both communities was from May 1992 to February 1993. Venous and cord blood samples were obtained at the time of delivery. After centrifugation, sera were stored at -70°C . A microneutralization assay previously described from this laboratory was used to determine the level of neutralizing antibodies to the two subgroups of RSV (15, 17). Plaque-purified RSV/Tracy (RSV/A) and plaque-purified RSV/18537 (RSV/B) were the viruses used in the assays. With each assay, maternal and cord blood paired sera were tested on the same microtiter plate. Antibody titers were expressed as the geometric mean titer (GMT) in log₂ \pm standard deviation.

Seventy-five maternal and 90 cord blood samples from The Gambia were tested, and of these 50 were maternal-newborn pairs. During a similar time interval, 110 maternal and 108 cord blood samples were obtained in Houston, of which 107 were maternal-newborn pairs. In less than 5% of specimens, the microneutralization assays for both RSV subgroups were not done because of the small volume of sera. Gambian mothers, who were mainly black, were distributed ethnically as follows: Jola, 36%; Madinka, 30%; Fula, 7%; Wollof, 5%; Sererre, 5%; and other ethnic groups, 17%. The study population in Houston consisted of 50% Caucasians, 28% African-Americans, 18% Hispanics, and 4% Asians. Mothers from Houston were significantly older than their Gambian counterparts (28.3 ± 6.0 years vs. 23.7 ± 6.1 years [mean \pm standard deviation], $P < 0.001$ by the Student *t* test).

Titers of neutralizing antibody to RSV/A and RSV/B are presented in Table 1. The titers of antibody to both RSV subgroups in the two communities were normally distributed.

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TABLE 1. RSV-neutralizing-antibody titers in sera of mothers and newborns from The Gambia and Houston at the time of delivery

RSV type	Serum source	GMT (\log_2) ^a		<i>P</i> value ^b
		Gambia	Houston	
A	Mothers	8.8 \pm 1.3 (75)	8.8 \pm 1.5 (106)	NS
	Newborns	8.3 \pm 1.4 (90)	8.8 \pm 1.5 (106)	0.02
B	Mothers	8.7 \pm 1.4 (75)	7.9 \pm 1.3 (106)	0.0001
	Newborns	8.7 \pm 1.3 (83)	8.0 \pm 1.6 (108)	0.001

^a Determined by the microneutralization test. Values are means \pm standard deviations. Values in parentheses are *n* values.

^b Differences between GMTs of mothers and newborns from The Gambia and those of mothers and newborns from Houston were determined with the two-tailed Student *t* test. NS, no significance.

Maternal sera from The Gambia and Houston had similar GMTs of antibody to RSV/A; however, Gambian mothers had significantly higher GMTs of antibody to RSV/B. Maternal age did not influence the GMT of antibody to the RSV subgroups in either population. Among Gambian mothers, those with fewer than three previous live births had higher GMTs of antibody to both RSV subgroups than those with three or more live births, although this was statistically significant only for RSV/B (9.0 ± 1.5 versus 8.2 ± 1.2 , $P < 0.05$ by the Student *t*

test). Parity did not influence the GMTs of antibody to the RSV subgroups in the mothers from Houston.

Neutralizing-antibody titers equal to or greater than $9 \log_2$ have been associated with protection against RSV disease (6, 8, 18). The proportions of mothers with a titer of neutralizing antibody to RSV/A of $9.0 \log_2$ or greater were similar in the two populations (The Gambia versus Houston; 48% versus 52%). However, Gambian mothers were significantly more likely to have antibody to RSV/B at this level than their counterparts in Houston (46%, versus 27%, $P = 0.01$ by χ^2 test). A greater proportion of Gambian mothers with fewer than three live births had titers of neutralizing antibody of $9.0 \log_2$ or greater for RSV/A (60% versus 33%, $P = 0.03$ by χ^2 test) and for RSV/B (53% versus 32%, $P = 0.09$ by χ^2 test) compared with Gambian mothers with three or more children. Parity did not influence the proportions of American mothers with this level of antibody. Also, significant differences were not observed among GMTs for the various ethnic groups in The Gambia or Houston.

The GMT of antibody to RSV/A was significantly higher in newborns from Houston, while Gambian newborns showed significantly higher GMTs of antibody to RSV/B (Table 1). Newborns in Houston born to young mothers (ages, <20 years) had a significantly higher GMT of antibody to RSV/B than did newborns of older mothers (9.0 ± 1.8 versus 7.8 ± 1.5 ,

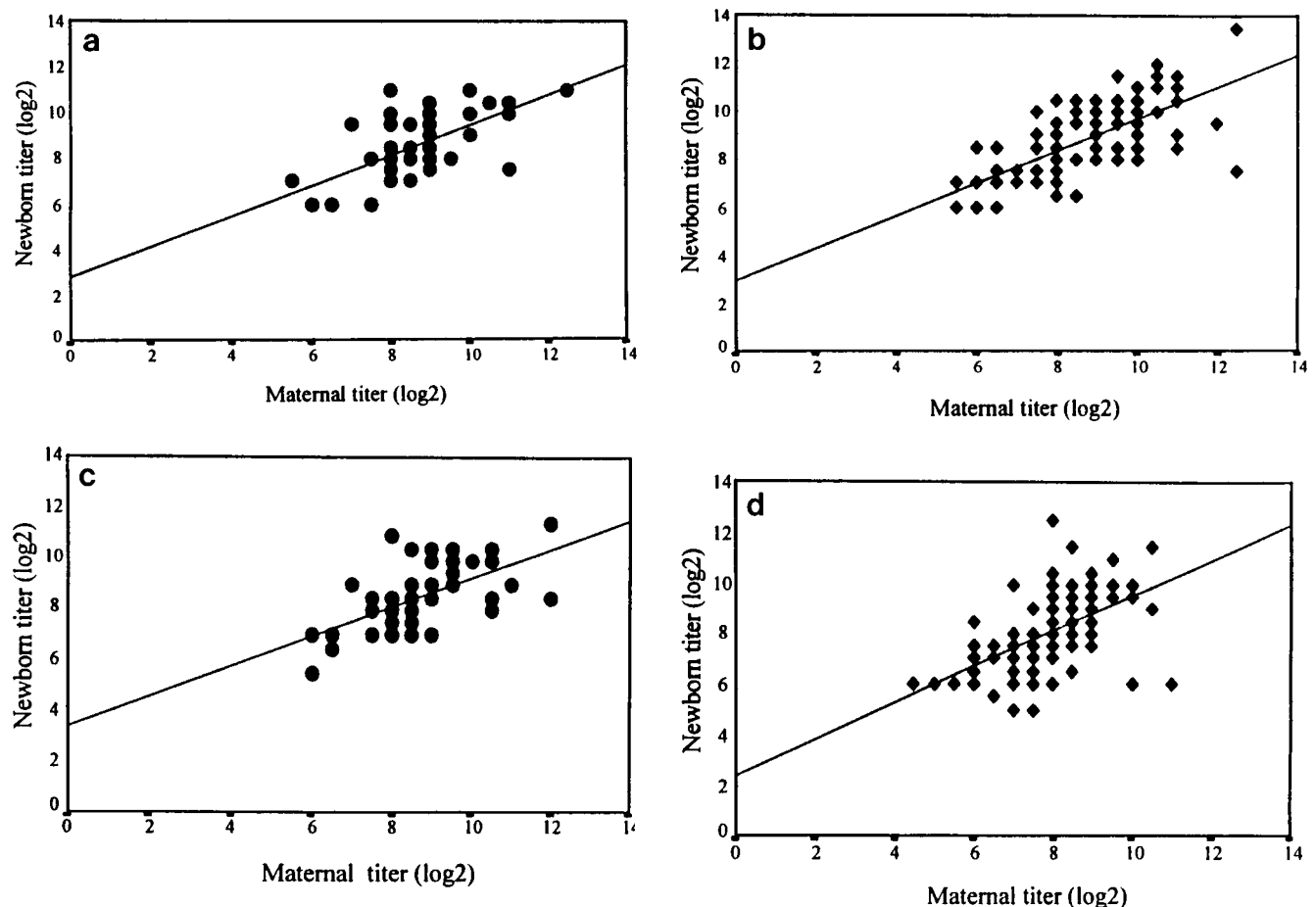


FIG. 1. Correlation of RSV-specific neutralizing-antibody titers in maternal-cord blood paired sera from The Gambia (a and c) and Houston (b and d). The Pearson correlation coefficients for neutralizing antibody to RSV/A for the maternal-cord blood paired sera were 0.6 in The Gambia (a) and 0.7 in Houston (b). The Pearson correlation coefficients for neutralizing antibody to RSV/B for the maternal-cord blood paired sera were 0.6 in The Gambia (c) and 0.61 in Houston (d).

$P = 0.02$ by the Student t test). Neither maternal age nor parity influenced the titer of RSV-neutralizing antibody in sera from Gambian newborns. The proportions of newborns with titers of neutralizing antibody to the RSV subgroups equal to or greater than $9 \log_2$ were not significantly different between the two populations.

The efficiency of antibody transfer from mothers to their newborns was analyzed with only maternal-cord blood paired sera. The ratio of RSV-specific neutralizing-antibody titers in newborns to those in mothers (GMT transmission) in The Gambia was 0.99 for each of the virus subgroups, while the ratios in Houston were 1.02 for RSV/A and 1.03 for RSV/B. In addition, the neutralizing-antibody titer of infants was significantly correlated to that of their mothers (Fig. 1).

In this study, the prevalences of neutralizing antibody to the major subgroups of RSV were comparable between the study populations in two geographically distinct areas, The Gambia and Houston. The antibody prevalence data support the studies that identified RSV as a common respiratory viral pathogen in both industrialized and developing countries (1, 2, 7, 9). They further suggest that the major RSV subgroups that cause outbreaks in industrialized countries are circulating in The Gambia and possibly other developing nations.

Efficient transfer of maternal neutralizing antibodies across the placenta was demonstrated by the GMT transmission ratio of newborn to mother of approximately 1.0 for both RSV/A and RSV/B. This is in contrast to what has been reported for antibody to bacterial polysaccharides such as meningococcus and *Haemophilus influenzae* type b; transplacental transmission of polysaccharide-specific immunoglobulin G antibody to the neonate is approximately 50% (5, 13). Maternal immunization during the third trimester of pregnancy with a safe and immunogenic RSV vaccine offers a way of boosting antibody titers. In particular, acquisition of virus-specific, maternal antibodies by the newborn has been associated with protection against RSV disease (11, 14). Furthermore, the use of high-titer intravenous immunoglobulin in high-risk children reduced the frequency of RSV lower respiratory tract disease, and in animal models it decreased virus replication in the lungs (8, 19).

Although the level of RSV-neutralizing antibody that is protective against severe RSV disease is not yet known with certainty, we chose a value of at least $9 \log_2$ (1:512) as a likely protective titer on the basis of studies in term infants and animal models (6, 8, 18, 19). The higher GMT of neutralizing antibody to RSV/A observed in sera of newborns from Houston and the higher GMT of antibody to RSV/B in sera from Gambian newborns are of interest. This may have biological significance when the RSV subgroups circulating in a given season are considered. In The Gambia, the dominant subgroup during the 1993-1994 RSV season was RSV/A; the high titers of neutralizing antibody to RSV/B during the 1992-1993 season may have selected for infection with RSV/A the following viral season. In Houston, RSV/A was the major circulating subgroup during the 1991-1992 season; the higher GMT of antibody to RSV/A might reflect the predominance of RSV/A during the 1991-1992 RSV season. Piedra et al. have presented data suggesting that a relationship exists between maternal-cord blood RSV-neutralizing-antibody titers and RSV subgroups circulating in the community (16). The hypothesis put forth was that the level of neutralizing antibody prevalent in mothers and their newborns will influence the RSV subgroup circulating in infants less than 6 months of age. Thus, if high titers of neutralizing antibody to RSV/B are prevalent in mothers and their newborns, RSV/A will then be the predominant virus circulating among infants.

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